Claims

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1. An compound selected from: a compound of Formula (I)

5 and a salt, solvate or physiologically functional derivative thereof, wherein:

R¹ represents hydrogen, halogen or C₁-C₃alkyl;

R² represents a 5 or 6-member aryl, heteroaryl, heterocyclic or alicyclic ring;

Z represents $-(CH_2)_q$ - ; -CH=CH- ; $-(CH_2)_pNHC(O)-$; $-(CH_2)_pNHC(O)NH-$; $-(CH_2)_pNHC(O)O-$; $-(CH_2)_pSO_2NR^3-$; $-(CH_2)_pNR^3SO_{2^-}$; $-(CH_2)_nO-$; $-C(R^4R^5)O-$ or -Y-W-X- ;

W represents a 5 or 6-member aryl, heteroaryl, heterocyclic or alicyclic ring;

X and Y, which may independently be present or absent, where present independently represent $-(CH_2)_q-$; -CH=CH-; $-(CH_2)_pNHC(O)-$; $-(CH_2)_pNHC(O)O-$; $-(CH_2)_pNHC(O)NH-$; $-(CH_2)_pSO_2NR^3-$; $-(CH_2)_pNR^3SO_2-$; $-(CH_2)_pC(O)-$; $-(CH_2)_pNH-$; $-(CH_2)_pO-$;

n represents an integer selected from 2, 3 and 4;

p represents an integer selected from 0, 1 and 2;

q represents an integer selected from 1, 2, 3 and 4;

R³ represents hydrogen or methyl; and

30 \mbox{R}^4 and \mbox{R}^5 , which may be the same or different, independently represent $\mbox{C}_1\mbox{-}\mbox{C}_3\mbox{alkyl};$

provided

- (i) that when R^1 is hydrogen, Z is $-(CH_2)_n$ –, and n is 2, then R^2 is other than parachlorophenyl or para-methylphenyl and
- 35 (ii) that a compound of Formula (I) is other than 2-(2-(((4-(phenyl)phenyl) amino)acetyl)amino)benzoic acid, 2-(2-(((4-phenyl)phenoxy)acetyl)amino)benzoic acid, 2-[[4-cyclohexylphenoxy)acetyl]amino]benzoic acid, 2-[[3-(4-yclohexylphenoxy)acetyl]amino]benzoic acid, 2-[[3-(4-yclohexylphenoxy]acetyl]amino]benzoic acid, 2-[[3-(4-yclohexylphenoxy]acetyl]amino]benzoic acid, 2-[3-(4-yclohexylphenoxy]acetyl]amino]benzoic acid, 2-[3-(4-yclohexylphenoxy]acetyl]amino]benzoic acid, 2-[3-(4-yclohexylphenoxy]acetyl]amino[[3-(4-yclohexylphenoxy]acetyl]amino[[3-(4-yclo

chlorophenyl)-1,2,4-oxadiazol-5-yl]-1-oxopropyl]amino]benzoic acid or compound X

- 5 2. A compound according to claim 1 wherein R¹ is hydrogen or methyl.
 - 3. A compound according to claim 2 wherein R¹ is hydrogen.
- 4. A compound according to any preceding claim wherein R² is cyclohexyl, phenyl,
 10 pyridinyl, pyrimidinyl, pyridazinyl and isoxazolyl.
 - 5. A compound according to any one of claims 1-3 wherein R² is selected from the group consisting of:

- 6. A compound according to any one of claims 1-3 wherein R² is substituted phenyl.
- 7. A compound according to claim 6 wherein R^2 is phenyl substituted with one or two substituents selected from halogen C_{1-3} alkyl, C_{1-3} haloalkyl C_{1-3} alkoxy and C_{1-3} haloakloxy.
- 10 8. A compound according to any preceding claim wherein Y is -O-, -CH₂- or -CH₂O-.
 - 9. A compound according to any preceding claim wherein X is absent or is −SO₂NR³−, −NHC(O)− or −NHC(O)NH−.
- 15 10. A compound according to any preceding claim wherein Y is $-CH_2$ and X is $-SO_2NR^3$.
 - 11. A compound according to any one of claims 1-7 wherein Y is -O- and X is absent.
- 20 12. A compound according to any preceding claim wherein W is a 5 or 6 member aryl or heteroaryl ring.
 - 13. A compound according to claim 12 wherein W is phenyl.

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- 14. A compound according to claim 12 wherein W is a 5 member heteroaryl ring.
- 15. A compound according to any preceding claim for use in human or veterinary medicine
 - 16. A compound according to any one of claims 1-14 for use in the treatment of disorders of lipid metabolism including dislipidaemia or hyperlipoproteinaemia or of inflammatory diseases or conditions.
 - 17. Use of compound according to any one of claims 1-14 in the manufacture of a medicament for the treatment of disorders of lipid metabolism including dislipidaemia or hyperlipoproteinaemia or of inflammatory diseases or conditions.
- 15 18. A compound selected from: a compound of Formula (Ia)

$$CO_2H$$
 R^2
 O
(la)

and a salt, solvate or physiologically functional derivative thereof, for use in the treatment of disorders of lipid metabolism including dislipidaemia or hyperlipoproteinaemia or of inflammatory diseases or conditions

wherein:

R¹ represents hydrogen, halogen or C₁-C₃alkyl;

25 R² represents a 5 or 6-member aryl, heteroaryl, or heterocyclic or alicyclic ring;

Z represents $-(CH_2)_n -$; -CH=CH-; $-(CH_2)_pNHC(O)-$; $-(CH_2)_pNHC(O)NH-$; $-(CH_2)_pNHC(O)O-$; $-(CH_2)_pSO_2NR^3-$; $-(CH_2)_pNR^3SO_{2^{--}}$; $-(CH_2)_qO-$; $-C(R^4R^5)O-OP-Y-W-X-$;

W represents a 5 or 6-member aryl, heteroaryl, heterocyclic or alicyclic ring;

X and Y, which may independently be present or absent, where present independently represent $-(CH_2)_q-$; -CH=CH-; $-(CH_2)_pNHC(O)-$; $-(CH_2)_pNHC(O)O-$; $-(CH_2)_pNHC(O)NH-$; $-(CH_2)_pSO_2NR^3-$; $-(CH_2)_pNR^3SO_2-$; $-(CH_2)_pC(O)-$; $-(CH_2)_pNH-$; $-(CH_2)_pO-$ or $-(CH_2)_pO-CH_2-$;

n represents an integer selected from 2, 3 and 4;

p represents an integer selected from 0, 1 or 2;

g represents an integer selected from 1, 2, 3 and 4;

R³ represents hydrogen or methyl; and

10 R⁴ and R⁵, which may be the same or different, independently represent C₁-C₃alkyl.

- 19. A compound according to claim 18 wherein the use is in the treatment of diabetic dyslipidaemia, mixed dyslipidaemia, heart failure, hypercholesterolaemia, cardiovascular disease including atherosclerosis, arteriosclerosis, and hypertriglyceridaemia, hyperlipidaemia, anorexia nervosa, obesity, coronary artery disease, thrombosis, angina, chronic renal failure, peripheral vascular disease or stroke.
- 20. Use of a compound selected from: a compound of Formula (la)

$$CO_2H$$
 R^2
 CO_2H
 R^2
 CO_2H
 R^2
 CO_2H
 R^2
 CO_2H
 R^2
 CO_2H
 R^2
 CO_2H
 CO_2H

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and a salt, solvate or physiologically functional derivative thereof in the manufacture of a medicament for the treatment of disorders of lipid metabolism including dislipidaemia or hyperlipoproteinaemia or of inflammatory diseases or conditions

wherein:

R¹ represents hydrogen, halogen or C₁-C₃alkyl;

R² represents a 5 or 6-member aryl, heteroaryl, or heterocyclic or alicyclic ring;

30 $Z \text{ represents } -(CH_2)_n - ; -CH=CH-; -(CH_2)_pNHC(O)-; -(CH_2)_pNHC(O)NH-; -(CH_2)_pNHC(O)O-; -(CH_2)_pSO_2NR^3-; -(CH_2)_pNR^3SO_2-; -(CH_2)_qO-; -C(R^4R^5)O-or-Y-W-X-;$

W represents a 5 or 6-member aryl, heteroaryl, heterocyclic or alicyclic ring;

X and Y, which may independently be present or absent, where present independently $-(CH_2)_q$; -CH=CH- ; $-(CH_2)_pNHC(O)-$; $-(CH_2)_pNHC(O)O-$; $-(CH_2)_pNHC(O)O (CH_2)_pNHC(O)NH-$; $-(CH_2)_pSO_2NR^3-$; $-(CH_2)_pNR^3SO_2-$; $-(CH_2)_pC(O)-$; $-(CH_2)_pC(O) (CH_2)_pNH-$; $-(CH_2)_pO-$ or $-(CH_2)_pO-CH_2-$;

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n represents an integer selected from 2, 3 and 4;

p represents an integer selected from 0, 1 or 2;

g represents an integer selected from 1, 2, 3 and 4; 10

R³ represents hydrogen or methyl; and

R⁴ and R⁵, which may be the same or different, independently represent C₁-C₃alkyl.

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21. A method for the treatment of a human or animal subject having disease characterised by under-activation of the HM74A receptor or in which activation of the receptor will be beneficial, which method comprises administering to said human or animal subject an effective amount of a compound selected from: a compound of Formula (la)

$$CO_2H$$
 R^2
 CO_2H
 R^2
 CO_2H
 R^2
 CO_2H
 R^2
 CO_2H
 R^2
 CO_2H
 CO_2H

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And a salt, solvate or physiologically functional derivative thereof wherein:

R¹ represents hydrogen, halogen or C₁-C₃alkyl;

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R² represents a 5 or 6-member aryl, heteroaryl, or heterocyclic or alicyclic ring;

Z represents $-(CH_2)_n -$; -CH=CH-; $-(CH_2)_pNHC(O)-$; $-(CH_2)_pNHC(O)NH-$; - $(CH_2)_0NHC(O)O-$; $-(CH_2)_0SO_2NR^3-$; $-(CH_2)_0NR^3SO_2-$; $-(CH_2)_0O-$; $-C(R^4R^5)O$ or-Y-W-X-;

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W represents a 5 or 6-member aryl, heteroaryl, heterocyclic or alicyclic ring;

X and Y, which may independently be present or absent, where present independently $-(CH_2)_0-$; -CH=CH-; $-(CH_2)_pNHC(O)-$; $-(CH_2)_pNHC(O)O-$; $-(CH_2)_pNHC(O)O-$; $-(CH_2)_pNHC(O)O-$; $(CH_2)_pNHC(O)NH-$; $-(CH_2)_pSO_2NR^3-$; $-(CH_2)_pNR^3SO_2-$; $-(CH_2)_pC(O)-$; 35 $(CH_2)_0NH_-$; $-(CH_2)_0O_-$ or $-(CH_2)_0O_-CH_2_-$;

n represents an integer selected from 2, 3 and 4;

p represents an integer selected from 0, 1 or 2;

5 q represents an integer selected from 1, 2, 3 and 4;

R³ represents hydrogen or methyl; and

R⁴ and R⁵, which may be the same or different, independently represent C₁-C₃alkyl.

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- 22. A method according to claim 21 wherein the condition is a disorder of lipid metabolism including dislipidaemia or hyperlipoproteinaemia or an inflammatory disease or condition.
- 23. A pharmaceutical formulation comprising a compound according to any one of claims 1-14 in admixture with one or more physiologically acceptable diluents, excipients or carriers.
- 24. A combination for administration together or separately, sequentially or simultaneously in separate or combined pharmaceutical formulations, said combination comprising a compound according to any one of claims 1-14 together with another therapeutically active agent.
- 25. A pharmaceutical formulation comprising a compound according to any one of claims
 1-14, plus a further active ingredient selected from the group consisting of statins,
 fibrates, bile-acid binding resins and nicotinic acid and one or more physiologically
 acceptable diluents, excipients or carriers.
 - 26. A method for the preparation of a compound of Formula (I)

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$$\begin{array}{c|c}
CO_2H & & \\
R^1 & & \\
\end{array}$$

$$\begin{array}{c|c}
Z & \\
R^2 & \\
\end{array}$$
(I)

in which R^1 represents hydrogen, Z represents -Y-W-X-, Y represents -(CH₂)_pO-, p represents the integer 1, and W, X and R^2 are as defined in claim 1, the method comprising the steps of:

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(i) amide bond formation by acetylation of an ester of anthranilic acid;

- (ii) addition of W or W-X-R² by substitution of a leaving group;
- (iii) deprotection of the anthranilic acid group;

and where desired or necessary converting a resultant free acid or base compound of Formula (I) into a physiologically acceptable salt form or vice versa or converting one salt form into another physiologically acceptable salt form.

- 10 27. A method according to claim 26 where in step (ii) comprises addition of W and a further step (ii)(a), addition of R², is included in the form of a further substitution reaction.
 - 28. A method for the preparation of a compound of Formula (I)

$$CO_2H$$
 N
 Z
 R^2
 O
 (I)

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the method comprising the steps of:

(i) formation of an amide between the amine group of 2-amino-bezoic acid and an activated acyl transfer reagent derived from a carboxylic acid

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(ii) where desired or necessary converting a resultant free acid or base compound of Formula (I) into a physiologically acceptable salt form or vice versa or converting one salt form into another physiologically acceptable salt form.

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